REMARKS

The Office Action of August 19, 2003 has been reviewed and the Examiner's comments carefully considered. Claims 13-18, 21 and 22 are currently pending in this application. In view of the following remarks, Applicant believe that all the asserted rejections are in condition for withdrawal and all the claims are in condition for allowance.

Claims 13-18 and 21-22 stand rejected under 35 U.S.C. § 112, first paragraph, for purported lack of enablement. The Examiner asserts that the invention encompasses anticipating the onset of muscle disuse syndrome, that the claims encompass prevention of a syndrome that has many potential causes such as aging, disease, physical handicaps, etc., and thus one would have to anticipate and envision every possible cause for the syndrome. The Examiner further asserts that to practice the invention one skilled in the art would have to first anticipate the onset of muscle disuse syndrome, the cause of the syndrome, the effective dosage, and duration of treatment in order to determine whether the disease is prevented.

The invention as claimed inheres in administering a creatine compound in unit dosage form during an immobilization period and a subsequent rehabilitation period. That is to say, administration of the creatine compound to prevent muscle disuse syndrome would not begin until an individual is immobilized, thus obviating the need to anticipate or envision onset of the syndrome beforehand. Further, there are substantial differences between muscle disuse syndrome and the disorders/diseases of muscle atrophy and muscle dystrophy. Muscle atrophy is designated as a myopathy and is a very specific muscular disease that results in a decrease in muscle fiber size in association with the progressive loss of myofibrils. Thus, muscle atrophy results in a permanent loss of skeletal muscle fibers that eventually is replaced with connective tissue. Muscle dystrophy defines a group of diseases that are also

designated as myopathies in which skeletal muscle tissue is destroyed. The muscle dystrophies are usually inherited, recessive diseases with very progressive courses, characterized by a degeneration of muscle cells resulting in atrophy with the eventual replacement of muscle tissue with connective tissue. In contrast to the above, muscle disuse syndrome is a temporal disorder caused by lack of neuromuscular stimulation due to lack of muscle activity which can be reversed if the affected muscle is exercised.

One does not have to know the cause of the syndrome, the effective dosage or the duration of treatment in order to determine whether a muscle disuse disease is prevented. First, the specific cause of muscle disuse syndrome in an individual, i.e, the reason why the particular individual is immobilized, is irrelevant because preventive treatment with the creatine compound of the present invention is begun at the time of immobilization which, by definition, always will proceed the onset of muscle disuse syndrome. Thus, whether the immobilization is due to aging, prolonged bed rest, chronic sedentary life-style, space travel, etc. is not relevant to the fact that sustained lack of muscle activity *per se* will result in muscle disuse syndrome. Second, the claimed invention indeed provides guidance with respect to the effective dosage and duration of creatine administration, namely "a total daily supplementation of about 5 to 20 g creatine," and "administering about 5 g creatine compound, in unit dosage form, more than once daily during the immobilization period and subsequently administering about 5 g creatine compound, in unit dosage form, only once daily during at least a portion of the rehabilitation period, wherein the rehabilition period lasts no longer than 10 weeks," as recited in claims 17 and 22, respectively. The specification thus provides enablement for one skilled in the art to practice the present invention.

Claims 13, 15-18 and 21 stand rejected under 35 U.S.C. § 102(b) for purported anticipation by Elgebaly. The Examiner asserts that Elgebaly teaches a method of restoring functionality in muscle tissue by administering cyclocreatine. The Elgebaly reference discloses a method for the prompt recovery of muscle tissue function, particularly muscle tissue such as the myocardium, subject to ischemia and post-ischemic reperfusion injury.

As described above, the invention as claimed inheres in preventing and treating a specific muscle disorder known as muscle disuse syndrome with the use of creatine compounds. Muscle disuse syndrome, as set forth in the claims, has a definite definition, i.e., a temporal disorder caused by lack of neuromuscular stimulation consequent to lack of muscle activity, which can be reversed if the affected muscle is exercised. Elgebaly does not disclose a muscular disease having this definition. Applicant appreciates that statements made herein will govern the construction of the claims. Applicant submits, therefore, that the Elgebaly reference neither teaches nor suggests the use of creatine compounds for preventing or treating muscle disuse syndrome as defined above, and thus cannot anticipate the present invention.

Claims 13-18 and 21 stand rejected under 35 U.S.C. § 103(a) for purported obviousness over Pischel et al. in view of Howard et al. The Examiner asserts that Pischel et al. teach a method of administering creatine ascorbates for enhancing muscular development as a prophylactic against and treatment for ischemia and muscular atrophy. The Examiner notes that Pischel et al. do not specify the dosage of creatine wherein the amount is decreased during treatment. The Examiner further asserts that Howard et al. teach a composition containing creatine in which the recommended supplementation is decreased after several days.

The Pischel et al. reference discloses the use of creatine ascorbate compounds for enhancing muscular development and strength in athletes engaged in sports, as prophylactics against ischemia, as immune system stimulants, and for treating muscular atrophy; and the Howard et al. reference discloses a creatine drink in the form of a powder or liquid for use as a supplement for human consumption.

Applicant notes that an essential feature of the Pischel et al. reference is creatine complexed with ascorbic acid to form creatine ascorbate, a compound which assertedly results in many of the beneficial effects disclosed therein. As the Examiner points out, Pischel et al. do not teach an effective dosage amount of creatine or decreasing the dosage amount during treatment.

As stated above, muscle disuse syndrome, as set forth in the claims, has a definite definition, i.e., a temporal disorder caused by lack of neuromuscular stimulation consequent to lack of muscle activity, which can be reversed if the affected muscle is exercised. Neither Pischel et al. or Howard et al. disclose a muscular disorder having this definition. Further, in contrast to the claimed invention, Pischel et al. disclose various general uses for their creatine ascorbate compound, such as promotion of muscular development in athletes or treatment of muscle atrophy, a disorder characterized by an irreversible loss of muscle tissue that eventually is replaced by connective tissue. Moreover, although Howard et al. disclose lowering the recommended amount of their creatine supplementation after four days, they also do not teach or suggest the particular effective dosages of creatine to prevent or treat muscle disuse syndrome of the present invention. Applicant submits, therefore, that neither Pischel et al. or Howard et al., alone or in combination, teach or suggest the new and unexpected results of the present invention,

wherein creatine is administered in effective dosage amounts beginning at the start of muscle tissue immobilization and continuing at decreased dosages during the rehabilitation period to prevent or treat muscle disuse syndrome.

Claims 13-14, 16-18 and 21-22 stand rejected under 35 U.S.C. § 103(a) for purported obviousness over XP-00210314 (Wyss et al.) in view of Howard et al. The Examiner asserts that Wyss et al. teach the use of oral creatine supplementation in muscle disease such as Duchenne and Becker muscular dystrophy, spinal muscular atrophy, etc. The Examiner points out that Wyss et al. do not specify the creatine dose, but that Howard et al. discloses the user of 20-30 g creatine per day for several days and that after that time no more than 2 to 3 g per day is necessary to maintain saturation of body stores.

Applicant reiterates that the invention as claimed inheres in preventing and treating a specific muscle disorder known as muscle disuse syndrome with the use of creatine compounds, which, as set forth in the claims, has a definite definition, i.e., a temporal disorder caused by lack of neuromuscular stimulation consequent to lack of muscle activity, which can be reversed if the affected muscle is exercised. None of the cited prior art discloses a muscular disease having this definition. Additionally, although Howard et al. disclose that the recommended amount of creatine supplementation may be decreased after several days, this would not render obvious the precise effective dosage amount of at least 5 g of creatine during the entire immobilization period which is decreased to 5 g during a portion of the rehabilitation period that lasts no longer than 10 days. Applicant contend, therefore, that one skilled in the art would not learn from Wyss et al. or Howard et al., alone or in combination, the new and unexpected finding that different effective dosage amounts of

creatine administration during immobilization and rehabilitation is efficacious for preventing or treating muscle disuse syndrome.

For all the foregoing reasons, claims 13-18, 21 and 22 are patentable over the cited prior art and in condition for allowance. Reconsideration of the rejections and allowance of all pending claims 13-18, 21 and 22 is respectfully requested.

Respectfully submitsted,

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